UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,194	06/02/2006	Johannes Bartholomaus	512100-2057	3326

20999 7590 04/29/2011
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
YU, GINA C	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
04/29/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,194	BARTHOLOMAUS, JOHANNES	
	Examiner	Art Unit	
	GINA C. YU	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-15 and 18-22* is/are pending in the application.

4a) Of the above claim(s) - is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-15 and 18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of amendment filed on February 9, 2011. Claims 1-6, 15, 18-22 are now pending.

The claim rejection made under 35 U.S.C. § 103 (a) as being unpatentable over Rupprecht et al. (US 6780504 B2) ("Rupprecht")in view of Becher (US 6153222) and Zerbe et al. (US 6177096 B1) ("Zerbe"), as indicated in the previous Office action dated September 9, 2010, is withdrawn and modified to address applicant's claim amendment.

The claim rejection made under 35 U.S.C. § 103 (a) as being unpatentable over Rupprecht in view of Becher and Lydzinski et al. (US 2003/0099692), indicated in the same Office action, is withdrawn and modified to address applicant's claim amendment.

In both rejections below, the original grounds of rejections are maintained.

Also in response to applicant's claim amendment, a new rejection is made under 35 U.S.C.§ 112, second paragraph as following.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites" the transmucosal or transdermal administration is buccal administration". However, as applicant has admitted in the specification, a buccal administration is limited to a transmucosal administration, as the buccal cavity is

composed of mucosal membrane only. The presently limitation that a transdermal administration can be a buccal administration is inoperable and factually incorrect.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-15, 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rupprecht et al. (US 6780504 B2) ("Rupprecht") in view of Becher (US 6153222) and Zerbe et al. (US 6177096 B1) ("Zerbe").

Rupprecht discloses a dosage form in a multi-layered film which contains an active ingredient, wherein the dosage form comprises a cover layer, at least one active ingredient-containing layer and an adhesive layer. See col. 1, line 53 - 67; instant claims 1, 9, 10, 18. Example 2 discloses such multi-layer film comprising 1 wt % prednisolone. See instant claim 22. The active ingredient-containing layer is formed from in-situ crosslinking of hydroxypropylmethylcellulose (MHPC), and tannin (a cross-linker) in water in presence of prednisolone. See Example 2, (b); see also Example 1; instant claims 1, 7. Rupprecht discloses to optimize the film properties by adjusting the ratio of polymer to crosslinking agent to from 1:1 to 4:1. See col. 3, lines 1-22; instant claim 21. The reference further teaches that the prior art multi-layer film dosage form allows the active ingredient to distribute uniformly over the whole layer, and that the

active ingredient-containing layer exhibits horizontal and/or vertical gradients of the respective active ingredient. See col. 3, lines 51 – 67; instant claims 11 and 19.

The active ingredients suitable for application of the prior art dosage film form include nutrients, analgesics, antiallergic agents, antibiotics, antiemetics, antiseptics, antihistamines, antihypertensive agents, appetite suppressants, cardiac remedies, chemotherapeutic agents, enzymes, hormones, immunomodulators, inoculations, local anesthetics, psychoactive drugs, spasmolytics, virustatics, vitamins, cytostatics, plant protection agent, growth promoter and/or fertilizer. See col. 4, lines 1-13; instant claims 7 and 8. Rupprecht teaches the prior art film is suitable in particular for use as a transmuosal medicament. See col. 8, lines 12 – 14; instant claims 1 and 15. Further including an additional barrier layer to the release side of the film to protect the release of the active agent is also taught. See col. 8, bridging par.; instant claims 13.

Rupprecht fails to teach adding glycerol in the active ingredient-containing layer of the film dosage form.

Becher teaches a dosage form in film of oral application, comprising a mixture of active ingredient, film former, and softeners. See abstract. The reference teaches using crosslinked carboxyvinyl copolymers and/or crosslinked polyvinyl pyrrolidone as film formers. See col. 2, lines 9-12. The reference teaches polyethylene glycol or glycerol as the softener. See Further substances. The film is supplied with release paper attached thereon, meeting the instant claims 9, 13, and 18.

Becher fails to teach the amount of glycerol as based on the total amount of crosslinked hydrophilic polymers.

Zerbe teaches a film containing therapeutic agents and/or breath freshening agent for use in the oral cavity. See instant claims 5 and 6. The film comprises water-soluble polymers selected from water-soluble cellulose derivatives and polyacrylates, among others. The reference teaches the film also contains one or more plasticizers. Example 1 teaches a dosage form in film form obtained from a composition comprising 6 g of glycerol and 30 g of hydroxypropylmethyl cellulose (20% of glycerol based on the total amount of the hydrophilic polymer). See instant claims 1 and 3. The suitable pharmaceutical actives for the oral dosage forms include psychoactive drugs, antihistamines, hormones, antibiotics, and chemotherapeutics. See col. 3, lines 16 – 33.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Rupprecht by employing glycerol as a softener or plasticizer for the film as motivated by Becher and Zerbe. The skilled artisan would have been motivated to do so because 1) Becher teaches dosage forms in film forms that utilize glycerol as a plasticizer and 2) Zerbe discloses the weight amount of glycerol used per the weight amount of film-forming polymers used in a similar formulations. Since Becher teaches adding glycerol with crosslinked film forming polymers, the skilled artisan would have had a reasonable expectation of successfully producing a stable film dosage form with improved and softened film properties.

Claim 1 requires the weight range of glycerol to from 30 % to 60 % by weight based on the total amount of crosslinked hydrophilic polymers. Generally, differences in concentration or temperature will not support the patentability of subject matter

encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this case, the utility of a plasticizer as a film softener is taught by Becher and Zerbe, and the latter teaches an operative weight amount of glycerol as plasticizer in a composition comprising a film forming polymer. Discovering by routine experimentations an optimal weight amount of the plasticizer for a different type of polymer such as the crosslinked hydrophilic polymer of Becher would take no more than ordinary skill of the art.

Claims 1, 6-15, 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rupprecht in view of Becher and Lydzinski et al. (US 2003/0099692).

Rupprecht and Becher are relied upon as discussed above.

Becher fails to teach the amount of the plasticizer.

Lydzinski teaches a dosage form in film form for delivering a variety of agents to a substrate, wherein the active agents may be pharmaceuticals such as dentifrice, antiseptics or agricultural agent such as fertilizers. See [0024]; Instant claims 6-8. The reference teaches plasticizers such as polyols, particularly glycerine, is used in "any desired amount" to increase the apparent flexibility of the film, although the prior art mentions using the plasticizer up to about 15 percent by weight of starch component which forms the bases for the prior art film form. See [0026].

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the teachings of Rupprecht by employing glycerol as a softener or plasticizer for the film as motivated by Becher and Lydzinski. The skilled artisan would have been motivated to do so because 1) Becher teaches dosage forms in film that utilize glycerol as a plasticizer and 2) Lydzinski discloses the specific weight amount of glycerol used per the weight amount of film-forming polymers used in a similar formulations. Since Becher teaches adding glycerol with crosslinked film forming polymers, the skilled artisan would have had a reasonable expectation of successfully producing a stable film dosage form with improved and softened film properties.

With respect to the weight amount of the plasticizer, since Lydzinski teaches plasticizers are used in any desired amount and to increase flexibility of the film, the skilled artisan would have been obviously motivated to find an optimal weight amount of the plasticizer to obtain the desired level of flexibility. Doing so by routine experimentations would have been well within the skill of the art according to the teachings and suggestions of the references.

Response to Arguments

Applicant's arguments filed on February 9, 2011 have been fully considered but they are not persuasive.

Applicant states, “none of Rupprecht, Becher, Zerbe and/or Lydzinski individually or collectively teaches" the claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking

references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, applicant focuses on deficiencies of secondary references and argues that Becher, Zerbe and Lydzinski each fail to teach in-situ crosslinked hydrophilic polymer of HPMC and tannin. Applicant is reminded that such the polymer is disclosed in the primary reference. The pending rejection is made over the teachings of Rupprecht in view of Becher, Zerbe and Lydzinski; the relevant issue is whether, in view of the teachings of the in-situ crosslinked polymers of HMPC crosslinked with tannin, the skilled artisan would have been motivated to incorporate glycerol in the film forming composition. Such issue could not be adequately addressed in the applicant's arguments, as the teachings of the primary reference has not been taken into consideration properly.

As discussed in the rejection, in-situ crosslinked hydrophilic polymers has been used for dosage film in pharmaceutical art, and using glycerol as a film softener for dosage film was also well known. It would have been prima facie obvious that a person of ordinary skill in the art would have used the same plasticizer to manipulate the in-situ crosslinked hydrophilic polymers of Rupprecht with a reasonable expectation of success. Nothing in the references teaches or suggests that the same plasticizer used for Becher or Zerbe or Lydzinski could not be used for the crosslinked polymers of Rupprecht.

Applicant asserts that the use of glycerol "as a plasticizer" in the present invention distinguishes the present invention from Rupprecht. Applicant is reminded

that a chemical composition and its properties are inseparable. See In re Spada, 911 F.2d 705, 709, 15 U.S.P.Q. 2d 1655, 1658 (Fed. Cir. 1990). The same compound which serves as a plasticizer in applicant's invention must also function as a plasticizer in the polymers of Rupprecht as well. The intent of applicant to use glycerol as a plasticizer does not serve a basis for patentability.

In the discussion of Becher, applicant urges the Office to dismiss the teaching of using glycerol as a softener (i.e., plasticizer) merely because the disclosure was under the heading of "further substance". Applicant's assertion is not persuasive, as the reference clearly teaches and suggests a person of ordinary skill in the art that glycerol is to be further incorporated to a hydrophilic crosslinking to soften, or plasticize the resulting film, just as applicant has done in this case. Applicant asserts that "Becher would not have directed one of ordinary skill in the art to a combination of glycerol as a plasticizer with in situ crosslinked hydrophilic polymers". However, the argument does not take into consideration that Rupprecht teaches of in situ crosslinked hydrophilic polymers in producing dosage film for delivery of active agents. Becher teaches that a plasticizer is conventionally used in formation of dosage film. A person of ordinary skill in the art would have been obviously motivated to *combine the teachings of the references* with a reasonable expectation that a plasticizer such as glycerol would be useful in manipulating the property of film which is formed in a in situ crosslinking polymerization.

Regarding Zerbe, applicant asserts that glycerol is used with non-crosslinking hydrophilic polymers rather than crosslinking polymers. However, a person of ordinary

skill in the art would have reasonably predicted that glycerol would not lose its inherent characteristic as a plasticizer for a film-forming polymer whether or not the polymerization is crosslinked. Applicant produces no evidence that a plasticizer which is useful to soften non-crosslinked polymers would be somehow expected to exert different properties or behave differently with crosslinked polymers.

Applicant also states that “Zerbe, like Becher, only mention glycerol in the context of broad classes of optional ingredients". Such statement is erroneous, as Becher explicitly teaches that glycerol is a film softener. It is unreasonable to assume that a person of ordinary skill in the art would have ignored such disclosure or unable to combine the teachings of Zerbe and Becher to deduce the amount of glycerol useful to soften a pharmaceutical dosage film.

Regarding Lydzinski, applicant states, "[g]lycerol is only mentioned as an example for polyesters". It is not clear what applicant means here. The fact that glycerol was employed for polyesters does not change the inherent characteristic of the same compound as a plasticizer. Nor would a person of ordinary skill in the art had any reason to believe that a plasticizer for polyesters would not be effective for the in-situ crosslinked hydrophilic polymers of Rupprecht.

Applicant states, “[p]lasticizers are normally employed in an amount of up to 20 % by weight based on the amount of polymer” without providing any support. Furthermore, applicant also has not taken into consideration that Lydzinski explicitly teaches "any amount" of plasticizers may be used to manipulate the flexibility of

resulting film. Given the expected end result of modified amount of plasticizers, optimization of the amount of glycerol is viewed prima facie obvious.

Applicant states, “[i]t is well known in the art that changing an element in polymer formulation can drastically affect the properties of the polymer formulation" and argues that there was no expectation of success in making changes to Rupprecht. In response, applicant is reminded that only *reasonable* expectation of success is needed to establish a prima facie case of obviousness.

Citing KSR v. Teleflex, Inc., applicant also states, "[t]he combination of Rupprecht, Becher, Zerbe and/or Lydzinski as applied in the Office action tends to the infinite”. See 550 U.S. 398, 82 U.S.P.Q. 2d 1385 (2007). It is not clear how applicant was able to conclude that choosing glycerol among the disclosed species of known plasticizers could be considered “the infinite”. All of the cited secondary references teach glycerol is a known plasticizer for film forming hydrophilic polymers. Selection of glycerol as a plasticizer would have been an obvious choice to a person of ordinary skill in the art.

Applicant asserts that evidence of unexpected results was shown in the present application. Applicant urges the Office to find "easy handleability" and "applicability to human skin and mucous membrane” an unexpected result of using glycerol in the topical film. In response glycerol has been used in topical formulations as evidenced by the cited references and as known in common knowledge, and its use in cosmetic and pharmaceutical compositions will not form a basis for patentability.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINA C. YU whose telephone number is (571)272-8605. The examiner can normally be reached on Monday through Friday, from 9:00AM until 5:00 PM..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GINA C. YU/
Primary Examiner, Art Unit 1617